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Flexibility of Sensory Representations in Prefrontal Cortex Depends on Cell Type

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SUMMARY

Discrimination tasks require processing, interpreting, and linking sensory information to the appropriate motor response. We report that neurons in prefrontal cortex (PFC) represent visual motion with precision comparable to cortical neurons at early stages of motion processing, and readily adapt this representation to behavioral context. We found that direction selectivity, recorded while the monkeys discriminated directions, decreased when they judged motion speed and ignored its direction. This decrease was more pronounced in neurons classified as narrow-spiking (NS) putative interneurons than in broad-spiking (BS) putative pyramidal neurons. However, during passive fixation, when the link between motion and its behavioral relevance was removed, both cell types showed a severe selectivity loss. Our results show that flexible sensory representation during active discrimination tasks is achieved in the PFC by a specialized neuronal network of both NS neurons readily adjusting their selectivity to behavioral context, and BS neurons capable of maintaining relatively stable sensory representation.

INTRODUCTION

Visually guided behaviors require processing, interpreting, and linking visual information to the appropriate motor action. Although the prefrontal cortex (PFC) has been strongly implicated in successful execution of such goal-directed behaviors (Miller and Cohen, 2001), relatively little is known about the way this region represents and interprets visual information used to guide behavior.

The prearcuate region of the PFC has direct connections with the majority of visual cortical areas (Barbas, 1988; Petrides and Pandya, 2007; Schall et al., 1995), and thus, is likely to receive direct information about visual attributes used in discrimination tasks. Indeed, visual responses in the PFC during tasks involving discrimination of arbitrary shapes or locations of visual targets have been well documented, and one of the most striking features of these responses, distinguishing them from visual responses at earlier stages of cortical processing, was their dependence on task demands (Asaad et al., 2000; Everling et al., 2002; Freedman et al., 2001; Rainer et al., 1998; Sakagami and Niki, 1994; White and Wise, 1999). This adaptability, one of the key characteristic of PFC neurons (Cohen et al., 1996), has also been observed in parietal cortex (Freedman and Assad, 2006; Toth and Assad, 2002), the region closely interconnected with the PFC (Medalla and Barbas, 2006). While these studies revealed striking flexibility in the way visual stimuli can be represented in PFC, the mechanisms underlying this important phenomenon are still poorly understood. The paucity of this information may be due in part to the relatively limited understanding of cortical mechanisms underlying shape selectivity.

In our study of the flexibility of sensory representation in the PFC, we focused on visual motion, one of the fundamental visual attributes with relatively well-understood neural processing. Recent recordings revealed high incidence of direction-selective responses in the PFC, strongly resembling those recorded in area MT (Zaksas and Pasternak, 2006), the region with which PFC has direct reciprocal connections (Barbas, 1988; Petrides and Pandya, 2007; Schall et al., 1995). The presence of the well-understood sensory selectivity provides a unique opportunity to explore the mechanisms underlying the flexibility of sensory representation in the PFC, and allows a meaningful analysis of the relationship of this adaptability to the properties of visual neurons it is likely to affect.

We examined this question by recording responses to identical stimuli during three different behavioral tasks—direction discrimination, speed discrimination, and passive fixation—and found remarkable flexibility in the selectivity for motion direction that was reflected in different ways in the behavior of neurons classified as either narrow-spiking (NS) putative interneurons or broad-spiking (BS) putative pyramidal neurons. NS neurons showed strongly reduced direction selectivity (DS) during the two tasks not requiring directional judgments (speed discrimination and passive fixation), while the selectivity of the BS neurons was most affected during passive fixation, when the monkeys were no longer required to actively engage in the task. One of the most striking observations was that during active shifts of attention from direction to speed, NS neurons matched their selectivity to the behavioral context while BS neurons maintained relatively stable representation of motion direction. Our results demonstrate the operation of mechanisms capable of enhancing or suppressing incoming sensory signals depending

on task demands, revealing an important role for PFC neurons in responding to sensory stimuli according to their behavioral relevance.

RESULTS

We recorded the activity of 168 neurons in PFC in two monkeys during three tasks—direction discrimination, speed discrimination, and passive fixation—involving identical random-dot motion stimuli. On each trial, all three tasks consisted of three periods: sample, delay, and test (Figures 1A–1C). In this paper we will focus exclusively on responses to visual motion presented during the sample and the test phases of the task.

Behavioral Tasks

During each recording session the monkeys performed three behavioral tasks, each cued by a different fixation target (see Figures 1A–1C) and run in blocks of ~200 trials. During each discrimination task, we measured accuracy thresholds by presenting sample and test stimuli with different speeds or directions, with values bracketing each animal's threshold, defined as the stimulus value corresponding to 75% correct performance (see Figures 1D and 1E). This allowed us to equate task difficulty and, during each task, to keep the overall percent correct of both monkeys approximately equal to each other. The analysis of each monkey's performance during the recording sessions revealed that for Monkey 1 the overall performance level was at 78% (±0.7; 57 sessions) and 77% (±0.69; 43 sessions) correct during the direction and the speed discrimination tasks, respectively. The performance of Monkey 2 on the two tasks was nearly identical, at 77% (±0.69; 33 sessions) and 78% (±0.71; 26 sessions) correct.

Cell Classification

In our analysis we took into account the well-established presence in the PFC, as in other cortical areas, of two morphologically and physiologically distinct classes of neurons, inhibitory interneuron and excitatory projection pyramidal neurons (Constantinidis et al., 2002; Mountcastle et al., 1969; Wilson et al., 1994). It has been shown that inhibitory interneurons can be distinguished from pyramidal neurons by the shorter duration of their action potentials, less response adaptation, and higher activity (Bartho et al., 2004; Connors and Gutnick, 1990; Contreras and Palmer, 2003; McCormick et al., 1985). Additional support for waveform duration-based classification came from an experiment showing that the pyramidal neurons providing direct projections to the superior colliculus were BS (Johnston et al., 2009).

We classified our neurons on the basis of their waveform duration by measuring the time between the trough and the peak of action potentials (Figure 1F) (Mitchell et al., 2007), and divided the neurons into two classes: NS with spike durations of <200 μs, and BS with spike durations >200 μs. In addition to the waveform duration, we accounted for the existence of a subclass of excitatory pyramidal neurons, "chattering" cells, with characteristics that overlap with those of inhibitory interneurons. This class of neurons differs from regular-spiking pyramidal cells with shorter-duration waveforms, higher mean activity, and a stereotypical pattern of bursting characterized by a bimodal interspike interval (ISI) histogram (Connors and Gutnick, 1990; Gray and McCormick, 1996; Nowak et al., 2003). To avoid misclassifying the chattering neurons, we examined ISI histograms of NS cells for signs of bimodality. This analysis revealed three neurons with bimodal ISI distribution, and these neurons were reclassified as BS neurons.

The population of average waveforms and the distribution of their durations are shown in Figures 1G and 1H. The NS neurons constituted 25% of the recorded neurons, a proportion in line with those in most previous reports (Constantinidis and Goldman-Rakic, 2002; Johnston et al., 2009; Rao et al., 1999). The data show a significant bimodal distribution of spike durations (Hartigan's dip test; $p = 0.02$; Hartigan and Hartigan, 1985) indicative of two distinct neuronal populations. Additional validation of our classification is the higher baseline activity of the NS neurons (median 17.2 spikes/s compared with 8.9 spikes/s; Mann-Whitney U test, $p = 0.002$) and higher firing rates in response to visual stimulation (median 32.9 s/s compared with 12.5 s/s; $p = 8.0\times10^{-7}$).

Recording Sites

The recording sites for neurons characterized in this study are shown in Figure 1I. The majority of these neurons were located in the prearcuate region of PFC, between the principal and the arcuate sulcus, with the larger proportion of neurons located in the ventral region.

Responses to Motion during the Three Tasks

We found that among 132 well-isolated neurons with significant task-related activity, 80% exhibited significant DS during the direction discrimination task, in response to the sample or the test. Among neurons that showed no significant DS during the direction task, only 5% were direction selective during the speed task. In this paper we focused exclusively on neurons with significant DS during the direction task.

Examples of Task Effects on Responses to Motion

Responses of three example neurons, two enhanced and one suppressed, to identical sample directions during the three tasks are shown in Figure 2. When the task changed from direction (left plot) to speed discrimination (middle plot), the activity of the neuron in Figure 2A, classified as a BS neuron (spike duration: 323 μs), changed little and it retained its stimulus selectivity. However, during passive fixation, its responses to the moving stimulus were no longer detectible and not reliably modulated by motion direction.

On the other hand, when the task switched from direction to speed, the example cell in Figure 2B (NS neuron; spike duration: 133 μs), fired more to the direction initially identified as the antipreferred one and reduced its response to the preferred direction, leading to reduced and reversed DS. During passive fixation, this neuron's antipreferred response increased nearly to the level of the preferred response and the neuron was no longer direction selective. The neuron in Figure 2C (BS; spike duration: 360 μs) showed strong direction-selective suppression during the direction task and became less selective during the speed and the passive fixation tasks. We should note that suppressive direction-selective neurons were relatively uncommon in our sample (18/89, 20%), with only three classified as NS.

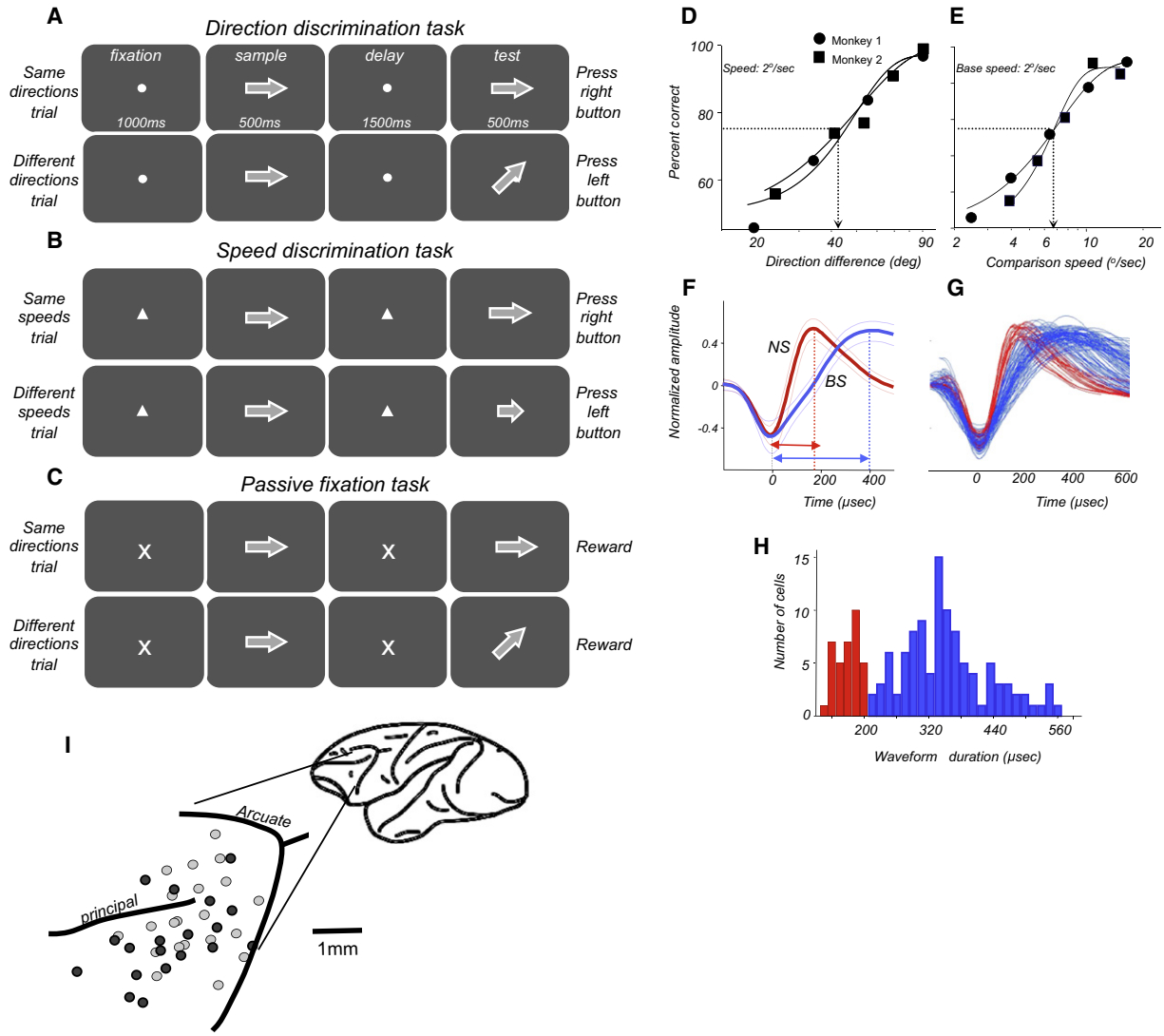

Figure 1. Behavioral Tasks, Behavioral Performance, Cell Classification, and Recording Sites

(A) *Direction discrimination task.* The animals reported whether the directions of motion of two random-dot stimuli separated in time, sample and test, were the same or different by pressing one of two response buttons. The top diagram shows a trial with the same directions (indicated by arrows) presented during the sample and the test. The bottom diagram shows a trial in which the two directions were different. During the task, the two types of trials were randomly interleaved and the differences in directions between the sample and the test were selected to bracket the threshold, defined as stimulus value taken at 75% correct (see D). The stimuli were centered on the fixation target (small circle) and the animals were required to maintain fixation within a 2° window throughout the trial. (B) *Speed discrimination task.* The animals fixated a small triangle and reported whether the speeds of the sample and the test were the same or different by pressing one of the two response buttons. The top and the bottom diagrams show the "same" and "different" speed trials, respectively. The shorter arrow in the bottom diagram indicates slower speed in the test. As in the direction task, the two types of trials were randomly interleaved and speed differences between sample and test were chosen to bracket the animal's threshold (see E). Sample and test always moved in the same (either preferred or antipreferred) direction. (C) *Passive fixation task.* Stimulus conditions were identical to those in the direction discrimination task. The monkeys were required to maintain fixation throughout the trial on a small cross and were rewarded after the offset of the second stimulus. (D and E) Representative psychometric functions for the two monkeys measured during the direction and the speed discrimination tasks. (F) Classification of neurons into narrow-spiking (NS) and broad-spiking (BS) cells. The duration of action potentials was estimated by measuring the time between the trough and the peak of each average action potential, as shown for the two example NS (red) and BS (blue) neurons. The thin lines indicate SEM. The value of 200 μs was used as the longest duration for the NS neurons. (G) Average action potentials of all recorded task-related neurons (n = 132) classified into NS (n = 29) and BS (n = 103) cells. (H) The distribution of action potential durations for these neurons was significantly bimodal (Hartigan's dip test, p = 0.02). (I) Locations of all direction-selective neurons recorded during the direction discrimination task. Lighter and darker circles indicate positions of neurons recorded from each monkey.

These examples illustrate the nonuniformity of the effects produced by the change in task demands. As we will show below, the relatively preserved DS exhibited by the BS neuron (Figure 2A) and the reduced DS of the NS neurons during the speed task (Figure 2B) are representative of the general behavior of neurons in our sample. We will also show that during

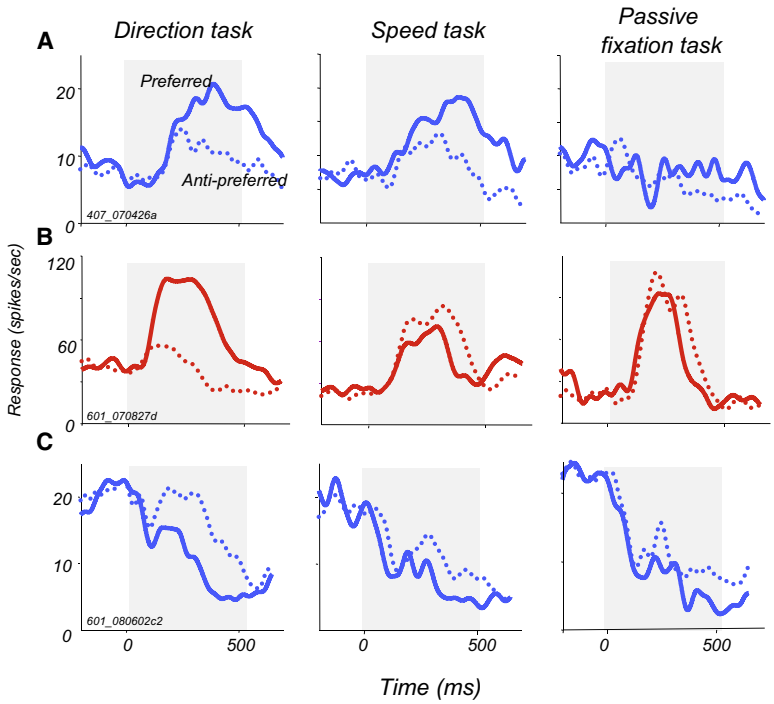

Figure 2. Example Responses to Motion during the Three Tasks

The plots show responses of each example neuron to identical moving sample stimuli presented during the direction (left plots), the speed (middle plots), and the passive fixation (right plots) tasks.

(A) Response of a BS neuron (spike duration, 323 μs) to the preferred and the antipreferred directions. This neuron's direction-selective response recorded during the direction task did not change substantially during the speed task (middle plot). During passive fixation, the responses to both directions decreased and were no longer direction selective.

(B) Response of this NS neuron (spike duration: 133 μs) to the direction identified as antipreferred during the direction task increased while its response to the preferred direction decreased. During passive fixation, the antipreferred response increased to the level of the preferred response, showing a complete loss of DS.

(C) Response of this BS neuron (spike duration: 360 μs) was suppressive, and during the direction task this suppression was less pronounced for the antipreferred direction. During the speed and the passive fixation tasks, the antipreferred response became more suppressed, approaching the response to the preferred direction, with the result of a greatly weakened DS.

passive fixation, both classes of neurons showed reduced selectivity, as illustrated by the behavior of the three example neurons.

Average Responses to Motion during the Three Tasks

The average response of all excitatory neurons in our sample to the preferred (solid line) and the antipreferred (dotted line) directions, plotted separately for NS (red) and BS (blue) neurons is shown in Figures 3A and 3B. During the direction task, the NS neurons responded at higher rates ($p = 8.0\times10^{-7}$) and both classes showed robust differences in their response to the two directions during the sample and the test. Figure S1 (available online) highlights the differences in selectivity measures between the two cell types. Briefly, both cell classes were equally likely to exhibit significant DS during the direction task (chi-square test, $p = 0.4$), and showed similar reliability in discriminating between the preferred and antipreferred directions (NS cells, area under the Receiver Operator Characteristic [ROC] curve [AROC] = 0.72; BS cells, AROC = 0.68; $p = 0.15$; Mann-Whitney U test). In addition, the tuning width of DS, measured during the search task, showed a trend toward a difference between the two classes of cells, with NS neurons exhibiting broader tuning, an observation consistent with broader tuning of this class of neurons for other sensory dimensions (Diester and Nieder, 2008; Nowak et al., 2008; Rao et al., 1999).

With the switch from the direction to the speed task, responses of NS neurons to preferred and antipreferred directions became more similar (Figure 3C), while BS cells continued to show robust stimulus selectivity during the sample, which weakened slightly during the test (Figure 3D). Finally, during passive fixation, responses of both classes of neurons to the two directions became more similar, illustrating the reduction in selectivity (Figures 3E and 3F).

Reduction in Direction Selectivity during the Speed Discrimination Task

We quantified these effects by computing DS with an ROC approach that allowed us to measure the probability with which, on the basis of firing rates, stimulus directions can be reliably classified as preferred or antipreferred (Britten et al., 1992; Green and Swets, 1966; Zaksas and Pasternak, 2006). The computed AROC served as a measure of DS. In this analysis, a value of 0.5 indicates a non-direction-selective response, i.e., that a given firing rate was elicited with equal probability by the two directions; a value of 1.0 indicates that responses to the preferred were always greater than responses to the antipreferred direction; and values lower than 0.5 indicate that the antipreferred response is greater than the preferred. We used this approach to evaluate the strength and the time course of DS during the direction (solid line) and the speed (dotted lines) discrimination tasks.

The data, plotted separately for NS (Figure 4A) and BS (Figure 4B) neurons, show clear differences in the behaviors of the two classes of neurons. The NS neurons exhibited a pronounced decrease in average selectivity during the sample and the test portions of the speed task compared with the direction task (significant periods indicated by thick red lines), while BS neurons showed only a modest task-dependent decrease in DS (Figure 4B). We should note that during the speed task, selectivity was not only weakened, but 15%–20% neurons of both types, classified as direction selective during the direction task, were no longer direction selective (Figures 4E and 4F). Thus, the plots in Figures 4A and 4B include the small proportion of neurons no longer direction selective. The comparison of task effects for the two classes of neurons, expressed as the difference between the direction-selective curves, is shown in Figures

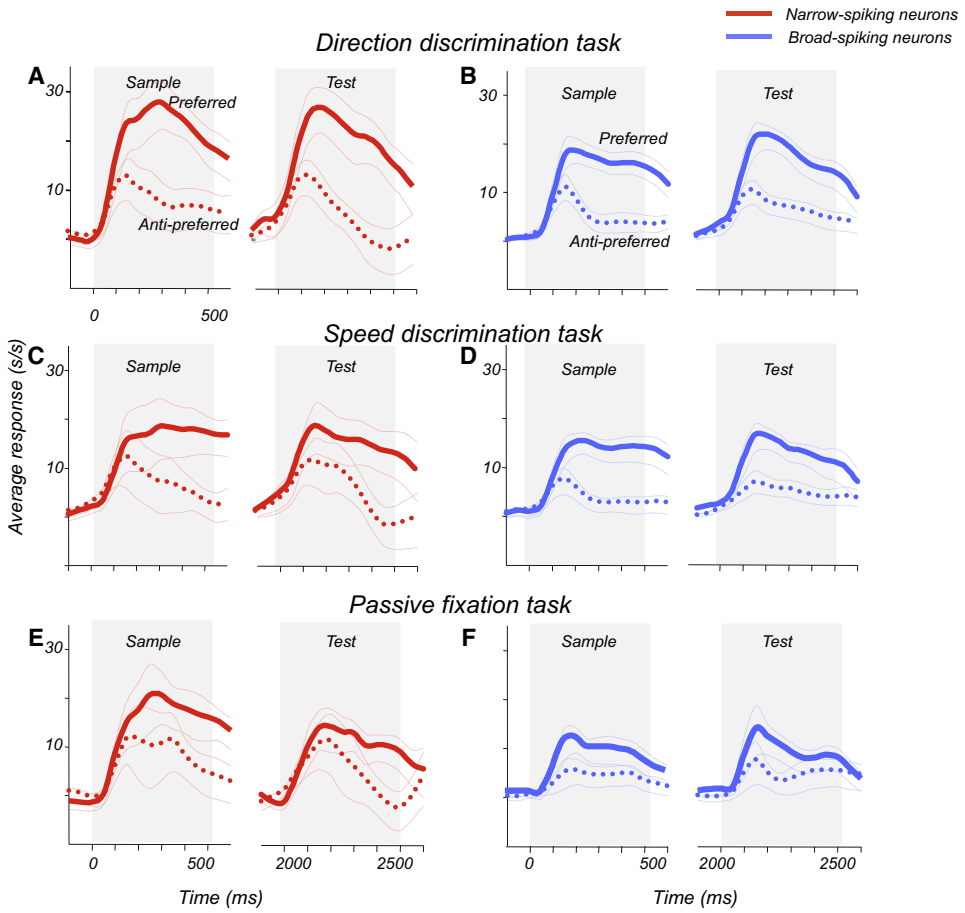

Figure 3. Average Responses to Motion during the Three Tasks

Average excitatory responses recorded during the direction discrimination task (A and B), the speed discrimination task (C and D), and the passive fixation task (E and F). Sample and test responses are shown separately for NS (red plots) and BS (blue plots) neurons. For each neuron, the mean baseline activity during the 200 ms prior to the onset of the sample was subtracted from the response. During the direction discrimination task, all NS neurons (sample, n = 17; test, n = 15) and BS neurons (sample, n = 44; test, n = 44) contributing to the data were direction selective (A and B). A subset of NS neurons (sample, n = 13; test, n = 14) and BS neurons (sample, n = 32; test, n = 36) tested in the direction task were also tested during the speed task (C and D). The data collected during passive fixation are based on responses of 10 NS and 23 and 20 BS neurons during the sample and the test, respectively. (E and F). Note that for NS neurons, the difference between responses to the preferred and the antipreferred direction, maximal during the direction task (A), decreased during the speed task (C), becoming minimal during passive fixation (E). For BS neurons, the difference between preferred and antipreferred activity changed little during the speed task (D), but decreased during the passive fixation (F). The thin lines on each plot show ±SEM.

4C. The data illustrate the relative preservation of DS for BS, compared with NS, neurons. The period of significant differences between the two curves is indicated by the solid gray lines along the x axis ($p < 0.05$, Mann-Whitney U test). The comparison of DS for individual neurons during the two tasks contributing to the average data, shown in Figure 4, can be found in Figures S2A and S2B.

The plots in Figure 4C indicate not only the differences in the size of the task effects between the two classes of cells, but also suggest the difference in the timing of these effects. We used two approaches to examine these differences. In one, we measured the latency of the task effect for the population of NS and BS neurons by a sliding significance test (see Experimental Procedures). During the sample, NS cells first showed a significant task effect about 100 ms before the task effect emerged in BS neurons (NS cells, 108 ms; BS cells, 212 ms). However, during the test the two cell classes showed more similar latencies (NS cells, 181 ms; BS cells, 171 ms). Although the differences in latencies observed during the sample are consistent with previous reports of longer latencies for putative pyramidal cells (Wilson et al., 1994), there is a possibility that the longer latencies of BS cells are due to their weaker task effects. We used an alternative approach to examine the time course of the task effects, and defined the latency as the point in time at which the task effect for the population reached half its maximum (see Experimental Procedures). This approach also revealed that the latency of NS cells preceded that for BS cells by 100 ms (NS cells, 115 ms; BS cell, 215 ms), although due to the small number of NS neurons, this difference failed to reach statistical significance ($p = 0.2$, two-sample bootstrap hypothesis test) (Efron and Tibshirani, 1993). Similar analysis applied to the task effects during the test confirmed the similarity

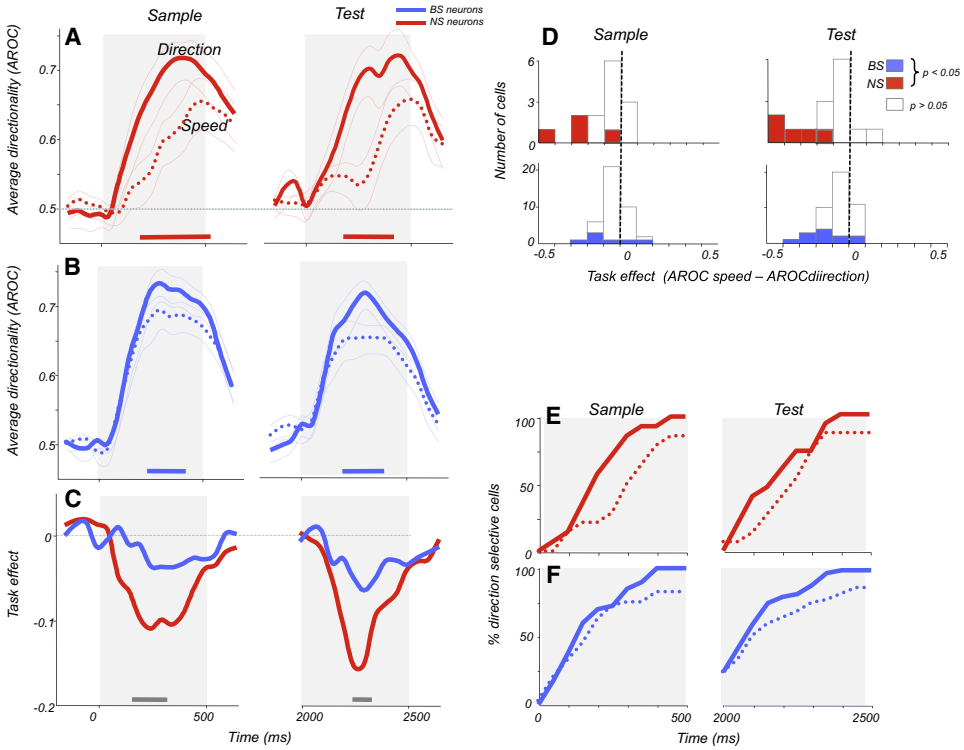

Figure 4. Reduction of DS during the Speed Task

(A) Average DS for NS neurons in response to the sample (n = 14) and the test (n = 15) during the direction task (solid red lines) and the speed task (broken red lines). DS, expressed as the area under the ROC curve (AROC), was computed by comparing firing rates to the two directions (see text). The data, representing responses of the same group of neurons tested during the two tasks, show a decrease in DS during the speed task. The period of significant differences in DS between the two tasks is indicated at the bottom of the graph by thick red lines. The differences were evaluated by sliding a 100 ms window every 50 ms during the course of both responses (Wilcoxon signed-rank test; $p < 0.05$).

(B) Average DS for BS neurons in response to the sample (n = 37) and the test (n = 41) recorded during the direction task (solid blue lines) and the speed task (broken blue lines). Thin pale lines indicate ±SEM.

(C) The task effect was computed for each neuron as the difference between DS curves computed during the two tasks and averaged. The task-induced change in DS was evaluated by sliding a 100 ms window stepped at 50 ms across the response and determining periods during which the DS was significantly different during the two tasks (Wilcoxon signed-rank test; $p < 0.05$). Thick gray lines below each plot indicate times at which the size of the task effect is significantly different between the two classes of neurons (Mann-Whitney U test; $p < 0.05$).

(D) Distribution of task effects shown in (C), measured during the period of 200–400 ms from stimulus onset. Neurons with significant task effects (ANOVA; $p < 0.05$) are indicated by red (NS neurons) and blue (BS neurons) columns, while the white columns show neurons with nonsignificant task effects. The area to the left of 0 (indicated by a dotted line) indicates a decrease in DS.

(E and F) Cumulative increase in the proportion of direction-selective NS (E) and BS (F) neurons after stimulus onset of the sample and the test during the direction (solid line) and the speed (dotted line) tasks. Note that between 15%–20% of NS (red) and BS (blue) neurons, classified as direction-selective during the direction task, no longer showed any significant DS during speed discrimination.

in latencies for the two cell classes (NS = 167 ms, BS = 159, p = 0.96, two-sample bootstrap hypothesis test). Taken together, these two analyses provide some evidence that during the sample, putative NS neurons show task-related decrease in DS earlier than putative BS cells. While this observation needs further confirmation, it is consistent with previous reports of differences in timing between putative inhibitory interneurons and pyramidal cells in the PFC (Wilson et al., 1994).

The behavior of direction-selective cells during the speed task shows that despite motion direction becoming irrelevant to the task, the majority of PFC neurons retained some degree of DS. One explanation for this preservation is that direction-selective neurons in MT, a likely source of selectivity in PFC (Zaksas and Pasternak, 2006), are also speed selective (Maunsell and Van Essen, 1983). Thus, it is likely that the representations of speed and direction in the PFC are also linked. In that case, during the speed discrimination task, which is likely to involve speed-selective neurons in MT and probably those in the PFC (Hussar et al., 2008), the direction-selective signals would not be completely "turned off."

Reduction of DS during the Passive-Fixation Task

The passive fixation condition allowed us to determine whether direction-selective activity persisted when the monkeys were not required to attend to visual stimuli, because the only behavior necessary for reward was maintaining fixation throughout both stimulus presentations. While the switch from the discrimination task represented a major change in task demands and removed

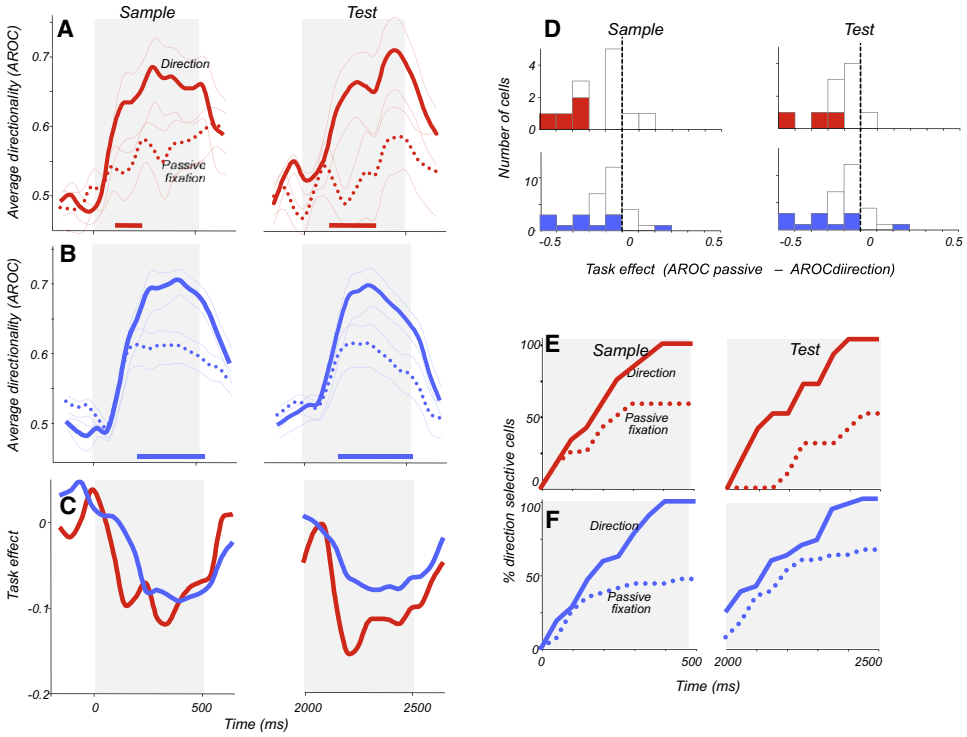

Figure 5. Reduction of DS during the Passive Fixation Task

(A) Average DS for the NS neurons in response to the sample (n = 12) and the test (n = 10) during the direction task (solid red lines) and the passive fixation task (broken red lines).

(B) Average DS for BS neurons in response to the sample (n = 32) and the test (n = 29) recorded during the direction task (solid blue lines) and the passive fixation task (broken blue lines). Thin pale lines indicate ±SEM.

(C) Average task effect for NS (red curve) and BS neurons (blue curve) showing a decrease in DS during the passive fixation task in both cell types.

(D) Distribution of task effects shown in (C), measured during the period of 200–400 ms from stimulus onset. Neurons with significant task effects (ANOVA; $p < 0.05$) are indicated by red (NS neurons) and blue (BS neurons) columns, while the white columns show neurons with nonsignificant task effects.

(E and F) Cumulative increase in the proportion of NS (E) and BS (F) direction-selective neurons after the onset of the sample and test during the direction (solid line) and the passive fixation (dotted line) tasks. For other details see the legend for Figure 4.

behavioral relevance from the stimuli, attention was not redirected elsewhere and it is conceivable that the animals would continue to evaluate motion, as in the direction task. However, the change in task demands resulted in a drastic change in neuronal activity (Figures 2 and 3; also see Figures S2D–S2F). Figures 5A and 5B provide a comparison between DS during the direction task and the passive fixation task for each class of neurons. They illustrate a profound loss of selectivity for both classes of neurons during passive fixation. This loss was much greater than that observed during the speed task ($p < 0.018$; Mann-Whitney U test; for a direct comparison of task effect between speed discrimination and passive fixation for cells recorded during both tasks, see Figure S3). It should be noted that the drastic drop in the average DS during passive fixation reflects the fact that about 50% of neurons of both types lost their DS during the passive fixation task (Figures 5E and 5F), a proportion substantially higher than that observed during the speed task (Figures 4E and 4F). Figure 5C illustrates the effect of the switch from the direction to the passive fixation task expressed as the difference between the direction-selective curves shown in Figures 5A and 5B. The distribution of task effects (Figure 5D) shows similarities in the behavior of both classes of neurons and a high proportion of cells displaying a significant loss of DS (shift to the left).

We were interested in whether the two classes of cells would differ in the time of onset of their task effects despite similar magnitude of these effects. The sliding significance method revealed that during the sample, NS cells reduced their DS about 100 ms before BS cells (NS cells, 109 ms; BS cells, 215 ms), the difference similar to that observed during the speed task. Interestingly, similarly to task effect during speed discrimination, during the test both classes of cells reduced their DS at about the same time (NS cells, 160 ms; BS cells, 165 ms).

These results demonstrate the severe weakening of direction-selective activity in both classes of cells during the task not requiring the use of visual stimuli to obtain the reward. They also show that BS cells appear to lag behind NS cells in exhibiting task-driven loss in DS.

Analysis of Task-Dependent Changes in Preferred and Antipreferred Responses

DS is an expression of the difference between a response to the preferred and to the antipreferred direction. Thus, lower DS could be the result of a weaker response to the preferred

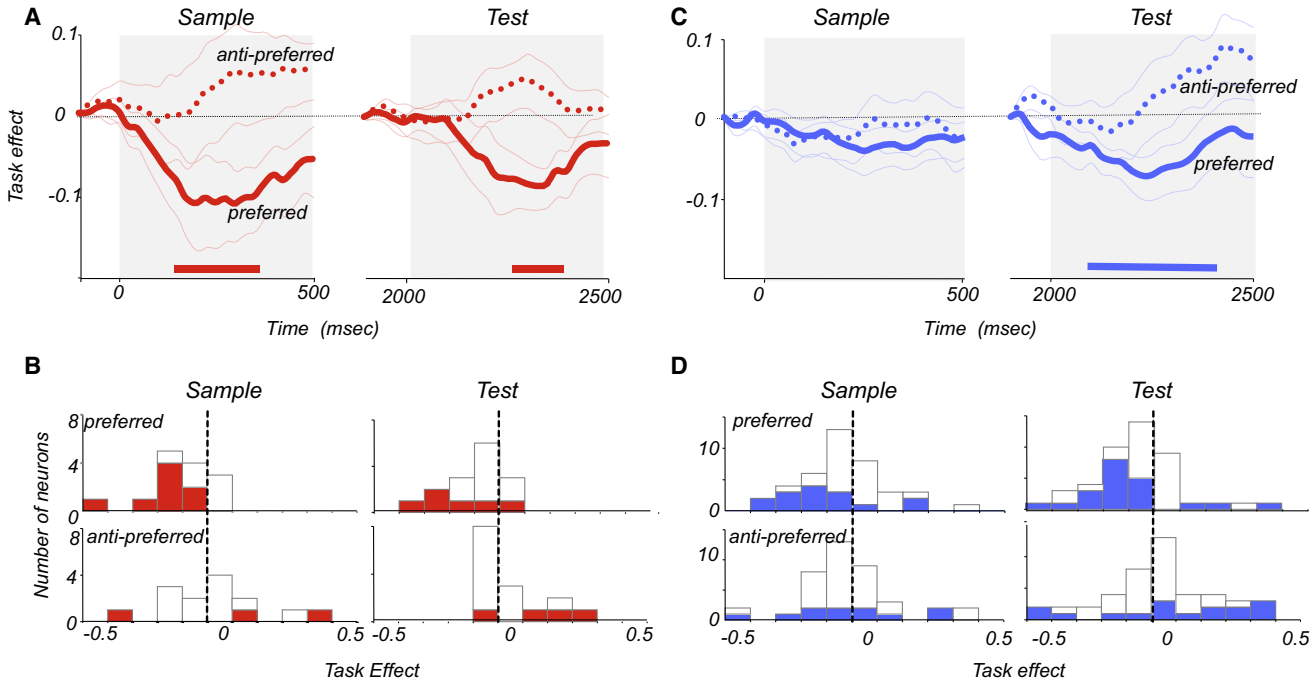

Figure 6. Changes in Preferred and Antipreferred Responses during the Speed Task

(A and C) Average task effects for NS (left plots) and BS (right plots) neurons computed separately for preferred (solid red or blue lines) and antipreferred (broken red or blue lines) directions. The task effect was computed as ($response_{speed} - response_{dir}$)/($response_{speed} + response_{dir}$). The task effect curve for each direction was generated by sliding a 200 ms window in 25 ms increments across responses generated during each task. Thick colored lines below each graph represent periods in which the task effect for the preferred or antipreferred direction was significantly different from 0 (Wilcoxon signed-rank test; $p < 0.05$). (B and D) Distribution of task effects for the preferred direction (top row) and antipreferred direction (bottom row) for individual neurons contributing to the data shown in (A) and (C). The data represent activity recorded during the period of 200–400 ms after stimulus onset. NS neurons with significant changes in activity are shown as red (Mann-Whitney U test; $p < 0.05$). The red columns correspond to the red lines and the pink columns to the pink lines in the plots shown in (A) and (C). Similarly, the blue columns correspond to the blue lines and the pale blue columns to the pale blue lines. BS neurons with significant changes in activity are shown as blue (preferred) and pale blue (antipreferred) columns (Mann-Whitney U test; $p < 0.05$). Thin pale lines indicate ±SEM.

direction, a stronger response to the antipreferred direction, or change in response to both directions. To determine which of these effects produced the observed selectivity loss, we determined the change in responses to each of the two directions when the task changed from direction to either speed or to passive fixation, and computed the task effect as follows: task effect index = ($response_{speed\ (passive)} - response_{direction}$)/($response_{speed\ (passive)} + response_{direction}$), where the subscripts "direction," "speed," and "passive" refer to the direction, the speed, and the passive fixation tasks, respectively.

Speed Discrimination Task

The comparison of preferred and antipreferred responses during the speed task to those recorded during the direction task provides insights into the nature of modulation of stimulus selectivity by the behavioral context (Figures 6A and 6C). NS neurons showed a decrease in the preferred response and a trend toward an overall increase in mean antipreferred activity (Figure 6A; thick red lines indicate periods of significance at $p < 0.05$; Wilcoxon signed-rank test). A closer look at the distribution of task effects for individual NS neurons revealed a clear shift toward reduction in the preferred activity (Figure 6B; top histograms; sample, $p = 0.013$; test, $p = 0.015$, Wilcoxon signed-rank test). The antipreferred direction elicited more variable task effects, with some neurons increasing their activity, some responding less, and some showing no change in firing rates (Figure 6B; bottom histograms; sample, $p = 0.49$; test, $p = 0.59$, Wilcoxon signed-rank test).

In contrast, the average response of BS neurons to each of the two directions changed little during the sample, although during the test they showed a greater task-dependent decrease in the preferred response (Figure 6C). The histograms showing task effects for individual BS neurons revealed that this apparent absence of the effect during the sample can be explained by the diversity of significant rate changes exhibited by these cells, with some neurons showing an increase and others a decrease (Figure 6D; preferred response, $p = 0.11$; antipreferred response, $p = 0.26$, Wilcoxon signed-rank test). On the other hand, during the test these neurons showed a significant decrease in the preferred response ($p = 0.01$, Wilcoxon signed-rank test) and no overall change in the average antipreferred response ($p = 0.31$, Wilcoxon signed-rank test). These data illustrate stronger and more consistent changes in activity to the preferred direction for the NS neurons. The apparently weaker effects on firing rates shown by BS neurons are in part a reflection of the nonuniformity of effects shown by many of these neurons. A closer look at the change in the preferred and antipreferred

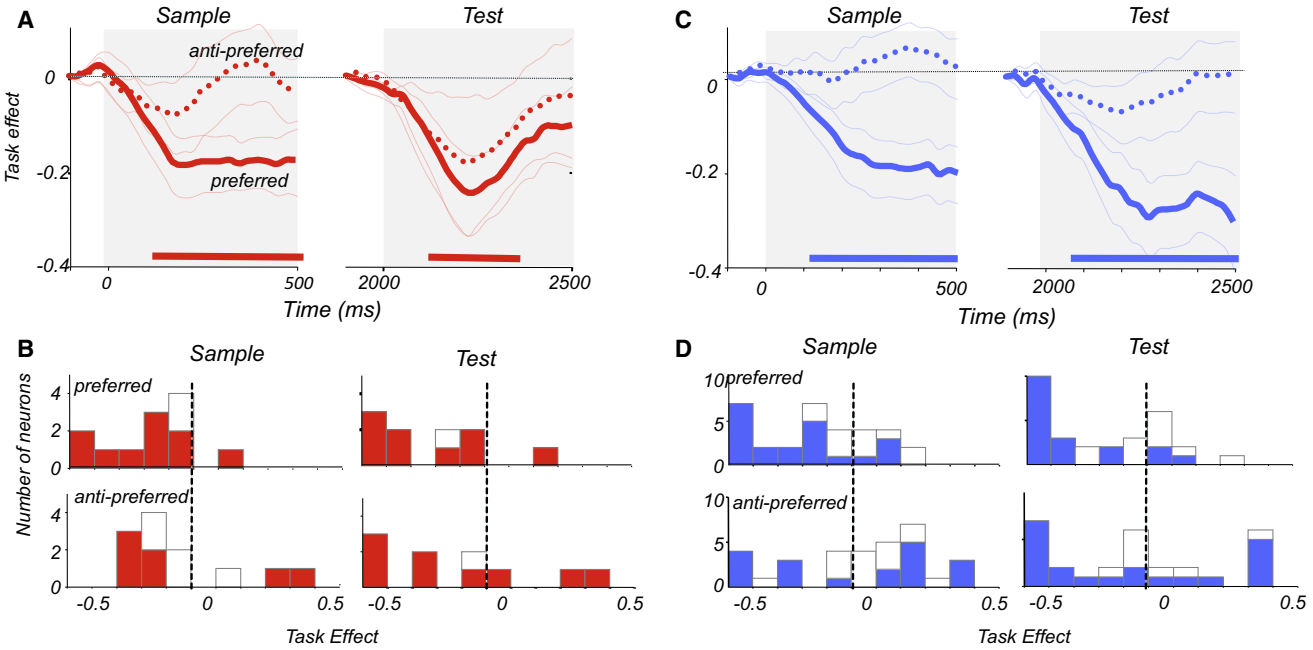

Figure 7. Changes in Preferred and Antipreferred Responses during the Passive Fixation Task

(A and C) Average task effects for NS and BS neurons computed separately for preferred (solid red and blue lines) and antipreferred (broken red and blue lines) directions. (B and D) Distribution of task effects for individual neurons contributing to the data shown in (A) and (C). For other details see the legend to Figure 6.

responses of PFC neurons on a cell-by-cell basis can be found in Figure S4. The data illustrate how the joint changes in response to both directions of motion result in the changes in DS shown above. During both tasks, the population of BS neurons showed a significant positive correlation between the changes in response to the preferred and antipreferred directions of motion (see figure legend of Figure S4 for details), a pattern indicative of a general change in gain. However, aside from their responses to the test during passive fixation, NS neurons showed no significant correlation between the changes in response to these two directions, suggesting differences in the mechanism by which these two types of neurons adapt to changing task demands. It is noteworthy that many neurons exhibited a decrease in the preferred response and an increase in the antipreferred response (cells in the upper left quadrant), an efficient change in activity for reducing selectivity. A related phenomenon of enhanced DS with attention directed to the neurons' preferred directions has been observed in area MT (Martinez-Trujillo and Treue, 2004). This enhancement was achieved by increasing responses to the preferred direction and decreasing responses to the antipreferred direction, a pattern reminiscent of the behavior of some neurons observed here.

The speed and direction discrimination tasks shared a number of key features, including identical random-dot stimuli, the "same" or "different" report rule, psychophysical procedure, identical consequences of incorrect and correct reports, and the motor response. Thus, the most likely explanation for the observed reduction in DS was a shift in the focus of the monkey's attention away from direction to another features of visual motion, its speed.

Passive Fixation Task

The analysis of average preferred and antipreferred responses, analogous to that performed for the speed task, revealed a more drastic reduction in the average response to the preferred direction for both types of neurons (Figures 7A and 7C), and this effect was most pronounced during the test. The frequency histograms (Figures 7B and 7D) show that the majority of NS and BS neurons significantly decreased their preferred responses. Although a number of neurons of both types also significantly decreased their antipreferred responses, these effects were balanced by other neurons increasing these responses. When averaged, these effects canceled each other, failing to reach statistical significance. A closer look at the behavior of individual neurons in response to the two directions (Figure S4B) reveals both similarities and differences in the behaviors of the two cell groups that depended on the period in the trial. During the sample, NS cells showed no correlation in the way they changed their responses to the two directions, a behavior similar to that observed during the speed task. In contrast, BS cells showed parallel and significantly correlated changes in their preferred and antipreferred responses, pointing to the operation of the gain mechanisms. During the test, however, both cell groups behaved similarly, showing strong positive correlations in their response to the two directions, i.e., they either increased or decreased their responses to both directions, a pattern indicative of a change in gain across tasks. These results illustrate that while putative pyramidal cells are more likely to be governed by gain mechanisms, the regulation of selectivity of NS cells is likely to be governed by several mechanisms, and these mechanisms can

be invoked dependent on the role visual stimuli play in a given behavioral task.

Task-Dependent Changes in Baseline Activity

In addition to changes in stimulus selectivity, we also observed small, but significant, task-dependent shifts in baseline activity recorded during the 200 ms before sample onset. The details of this analysis can be found in Figure S5. Briefly, BS, but not NS, neurons showed a significant increase in average baseline activity (from 12.2 to 14.2 s/s) during the speed task (BS: $p = 0.02$; NS = 0.33, Wilcoxon signed-rank test). This increase in baseline activity in BS cells may be indicative of the change in the attentional state of the monkeys when they were required to attend to motion speed rather than its direction.

Although during passive fixation neither cell class showed a significant change in the average baseline activity (BS: $p = 0.92$; NS = 0.07, Wilcoxon signed-rank test), individually, many cells (72% BS cells and 50% NS cells) exhibited significant changes in baseline firing rates (see Figure S5D, filled histograms, $p < 0.05$; Mann-Whitney U test). Among NS neurons, all but one cell showed a decrease in activity. On the other hand, BS cells were less consistent, with approximately equal numbers of cells increasing (38%) or decreasing (34%) their baseline rates.

While the observed effects are consistent with previous reports of changes in baseline activity in cortex congruent with task demands (e.g., Luck et al., 1997), we should note that each task was cued by a different fixation target (direction task, square; speed task, triangle; passive fixation, cross). Thus, the observed baseline activity may have been influenced not by the change in the behavioral task but by the change in the shape of the fixation target. However, the selectivity of these effects argues against this possibility. Specifically, during the speed task, the change in baseline activity was limited to BS neurons, an effect that would require these neurons as a group to prefer small triangles over small squares used to signal the direction task. A similarly unlikely scenario applies to the observed decrease in baseline activity for NS cells during passive fixation, since it is highly unlikely that these neurons as a group would show a preference for squares over crosses. Thus, the observed change in baseline activity with the change in task demand is unlikely to be related to different shapes of fixation targets during different tasks. In conclusion, these observations further highlight the differences in the behaviors of the two classes of cells during tasks placing different demands on the animals.

Sequence of Behavioral Tasks

To determine whether the selectivity for motion direction during the direction task was also present during the other two tasks, the activity during these tasks always had to be compared to responses recorded during the direction task. We optimized the likelihood of always having the data for such comparisons by starting each recording session with the direction task. This paradigm, however, created a potential problem of time-dependent changes in firing rates that could have contributed to the decreased stimulus selectivity during tasks introduced later in the recording session. To examine this possibility we compared firing rates and DS recorded during the first and the last 15 trials for 75 sample-responsive cells used in the main analysis and during the direction task (Figure S6). This analysis revealed no significant differences in either firing rates (NS: $p = 0.18$; BS: $p = 0.74$, Wilcoxon signed-rank test) or DS (NS: $p = 0.97$; BS = 0.72, Wilcoxon signed-rank test) between the early and late trials, arguing against the possibility that the reduction in DS during the speed and the passive fixation tasks are due to time-dependent changes in firing rates. Another argument against time-dependent effects playing a role in our results is the difference in the behaviors of NS and BS neurons during the speed task. Any bias due to the elapsed time should have affected both cell types equally, and this was not found. Finally, we found no evidence that the stability of recordings declined more for NS than for BS neurons. Specifically, when we were able to hold cells long enough to record during all three tasks, the proportion of NS to BS neurons was similar (30%, see Figure S3) to that recorded during any task (25%). Thus, it is unlikely that the sequence in which the tasks were introduced was responsible for the observed loss of DS during tasks not requiring directional judgments.

DISCUSSION

We found that the selectivity for stimulus direction in the PFC was strongly modulated by task demands and that the nature of this modulation differed between the NS and the BS neurons. DS recorded in response to moving stimuli during the direction discrimination task was lower when the same stimuli appeared during the speed discrimination task in which stimulus direction was irrelevant. This decrease in DS was greatest and most consistent in NS neurons. BS neurons were less affected by the change from the direction to the speed discrimination task, retaining a more stable representation of motion direction. The analysis of changes in the preferred and the antipreferred activity underlying the observed changes in DS revealed differences in the way the two classes of cells regulated their selectivity. Without exception, NS neurons showed independent modulation of responses to the preferred and the antipreferred directions. In contrast, BS cells tended to change their activity in parallel, showing strong positive correlation, either increasing or decreasing their responses to the two directions.

Cell Classification

Our approach to distinguishing between putative inhibitory interneurons and putative pyramidal neurons relied primarily on the differences between waveform durations in these two cell types, a measure suggested by intracellular recordings and confirmed by other approaches (Connors and Gutnick, 1990; Gray and McCormick, 1996; Nowak et al., 2003; Johnston et al., 2009). In our cell classification we took advantage of a bimodal distribution of waveform durations, similar to that reported in other extracellular recording studies (Chen et al., 2008; Constantinidis and Goldman-Rakic, 2002; Johnston et al., 2009; Mitchell et al., 2007; Diester and Nieder, 2008). Additional support for the distinction between the two classes of cells on the basis of waveform durations is provided by characteristic differences in their baseline and response firing rates, with putative interneurons showing significantly higher activity. We should point out, however, that the relationship between the duration of action

potentials and cell type does not hold for all neurons, and some pyramidal neurons with characteristically bimodal bursty firing patterns, the chattering cells, have been shown to have short action potentials (Connors and Gutnick, 1990; Gray and McCormick, 1996; Nowak et al., 2003). In our analysis, we examined ISIs and identified three such NS chattering cells, grouping them with the BS cell class. In sum, while the correspondence between waveform duration and cell class is unlikely to be one-to-one, our data based on this classification, along with other recent extracellular recording studies (e.g., Diester and Nieder, 2008; Johnston et al., 2009; Mitchell et al., 2007), reveal compelling functional differences between NS and BS cortical neurons.

Representation of Visual Motion in PFC

The selectivity for motion direction emerges first in primary visual cortex (Hubel and Wiesel, 1962) and is encountered in visual neurons at several levels of cortical visual processing, including motion processing area MT (for review see Pasternak et al., 2003). In visual neurons, the response to the preferred direction is likely to be mediated by the excitatory NMDA receptors, and the antipreferred response is likely to rely on active GABAergic inhibition of the NMDA-dependent process (Rivadulla et al., 2001; Sillito, 1975; Thiele et al., 2004). Selectivity for motion direction recorded in the PFC shares many characteristics with selectivity recorded in visual cortical neurons, and it is likely that rather than being generated de novo, DS in PFC is inherited from such neurons (Zaksas and Pasternak, 2006). While the mechanism by which PFC neurons modulate their DS is not known, it is conceivable that the responses mediated in visual neurons by excitatory NMDA receptors may also rely on a similar mechanism in the PFC. This idea is supported by the documented involvement of GABAa inhibition in spatial tuning of PFC neurons (Rao et al., 2000) and the possibility that the excitatory NMDA receptors implicated in other aspects of PFC activity (Compte et al., 2000) may be contributing to the modulation of the preferred responses.

We found that the incidence of DS was similar in the two classes of cells, although there was a trend in the activity of NS toward more reliable direction-selective signals. This observation is in agreement with a recent report that NS neurons in the PFC more reliably distinguished between different numerical categories (Diester and Nieder, 2008). Another distinguishing characteristic of NS neurons in the PFC has been their broader spatial tuning (Constantinidis and Goldman-Rakic, 2002; Diester and Nieder, 2008). We also found that NS neurons tended to have broader tuning for motion direction, a property also observed in direction-selective NS neurons in area V1 (Cardin et al., 2007; Nowak et al., 2008). This suggests that the observed representation of visual motion shares its characteristics with the representation of direction in motion processing neurons as well as with other sensory dimensions represented in the PFC.

Flexibility of Selectivity for Visual Features

The observed effects of behavioral relevance on stimulus selectivity are in line with previous reports of strong modulation of visual responses in the PFC during tasks requiring active shifts of attention between stimulus features (Asaad et al., 2000; Everling et al., 2002; Mansouri et al., 2007; Sakagami and Niki, 1994). These studies reported that about a third of PFC neurons were affected by the behavioral context. Although these previous studies have not distinguished between neuronal classes, it is tempting to speculate that many of the neurons modulated by attentional shifts may have belonged to the class identified here as NS. Indeed, the greater sensitivity of NS neurons to attentional demands has recently been observed in areas V1 (Chen et al., 2008) and V4 (Mitchell et al., 2007).

The presence of DS in the PFC and the nature of its adaptation to the behavioral context suggests the origins of feature-based attention effects observed in motion processing neurons in area MT by Martinez-Trujillo and Treue (2004). These investigators found that when attention was directed to the preferred direction, MT neurons enhanced their response to that direction and weakened their antipreferred activity, the pattern of modulation also observed in the activity of many PFC neurons. Thus, this type of modulation could be driven by direction-selective PFC neurons, many of which regulate their selectivity by independently changing their responses to the two directions (see Figure S4).

The properties of putative inhibitory interneurons and their interactions with putative pyramidal neurons in the PFC have been studied in monkeys performing oculomotor delayed response tasks (Rao et al., 1999; Wilson et al., 1994). These studies showed that both classes of neurons can carry specific spatial signals and that the adjacent interneuron/pyramidal pairs can share spatial preferences (Rao et al., 1999), and demonstrated the importance of GABAergic inhibition to the spatial selectivity characteristic of the pyramidal neurons in PFC (Rao et al., 2000). Our study demonstrates that both classes of neurons represent the direction of visual motion and suggests a role for NS neurons in signaling changes in the behavioral relevance of a given stimulus feature. BS neurons showed a modest decrease of DS during speed discrimination, but a robust loss during passive fixation. In the two discrimination tasks, the behavioral rule (‘‘same’’ or ‘‘different’’) was identical, and only the relevant sensory feature to which that rule was applied differed (direction versus speed). On the other hand, during passive fixation the behavioral rule did change and the link between the visual motion, the motor response, and the reward was removed. We found that BS neurons showed relatively modest changes in DS while the response rule remained unchanged, but exhibited strong effects during passive fixation when motor responses signaling the perceptual decision were no longer required. In contrast, NS neurons showed strong modulation of DS whenever direction was not relevant to the task. This observation can be seen clearly in Figure S3, showing DS recorded from the same group of neurons during the three tasks. During the speed discrimination task, DS of BS neurons was similar to that recorded during the direction discrimination task, highlighting their relative preservation of DS in tasks involving behaviorally relevant motion. For NS neurons, DS during speed discrimination was most similar to DS during passive fixation, illustrating their sensitivity to the behavioral context. This generalized sensitivity of NS neurons to behavioral context suggests a key role for interneurons in integrating sensory information with that information’s behavioral relevance in the PFC. One possible scenario is that the activity of BS neurons was influenced by NS neurons. Although our data

provide no direct information about interactions between the two classes of cells, such interactions have been reported (Rao et al., 1999; Wilson et al., 1994).

It is interesting to note that despite significant changes in their preferred and antipreferred responses (see Figure 6D), BS neurons retained relatively stable representation of direction during active shifts of attention from direction to speed. This observation sheds light on the nature of top-down motion signals arriving in visual cortex during motion discrimination tasks. It is possible that stable direction-selective, top-down PFC signals reaching motion processing cortical neurons are needed to ensure normal responses to stimulus speed and direction during discrimination tasks.

In conclusion, our study provides new insights into the way different classes of PFC neurons adjust their sensory representation to the behavioral context. It remains to be seen whether and how this flexibility is reflected in the top-down influences on the activity of cortical neurons directly involved in processing sensory signals used in discrimination tasks.

EXPERIMENTAL PROCEDURES

Subjects

We recorded from two adult male rhesus macaque monkeys. Water was restricted for 20 hr prior to each daily experiment, and the daily water rations were provided during the testing sessions. Experiments were carried out in accordance with the guidelines published in the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the University of Rochester Committee for Animal Research (UCAR).

Visual Stimuli

The stimuli and the behavioral tasks were similar to those used in previous studies from this laboratory (Zaksas and Pasternak, 2006). Stimuli were presented on a video monitor (19 inch Iiyama Vision Master Pro 513, running at 1152 X 870 pixel resolution and a 75 Hz refresh rate) placed 57 cm in front of the monkeys. Stimuli consisted of random dots placed in a circular 4° aperture, and their density was set at 4.7 dots/deg^2. The dots were 0.03° of visual angle in diameter with a luminance of 15 cd/m^2, shown on a dark background of 0.1 cd/m^2. Each dot persisted for the entire duration of the stimulus. The stimuli appeared at the center of the display and the monkeys were required to fixate a small target placed in the middle of the stimulus. Their fixation was maintained within a 2° electronic window and their eye position was monitored with an infrared eye-tracking device (ISCAN, Inc.).

Behavioral Tasks

Search Task

Each recording session began with a search task in which the monkey performed a coarse direction discrimination task. In this task, sample directions were chosen at random from the set of eight around the clock, and the test moved either in the same direction or in the orthogonal direction (90° difference). Neurons were isolated during the search task (see below for cell selection criteria).

Sequence of Behavioral Tasks

Once the preferred direction was identified during the search session, recordings always began with the direction discrimination task. The sequence of the other two tasks, the speed discrimination and passive fixation, was varied. In some recording sessions, a given cell could not be held long enough to record activity during all three tasks. In these cases the data were collected only for two of the three tasks, always including the direction discrimination task.

Direction Discrimination Task

During this task (Figure 1A), which is cued by a small fixation target, the animals compared two stimuli separated by a brief (1500 ms) delay, sample and test, moving coherently at the same speed. On each trial, the directions of sample and test either differed by 90° or less or were the same, and the set of directions during each session always included preferred and antipreferred for a given neuron. During each recording session direction differences between sample and test were chosen to bracket each animal's threshold, defined as the direction difference corresponding to 75% correct performance. Example psychometric functions for the two monkeys, shown in Figure 1D, illustrate typical performance on direction discrimination during recording sessions. Throughout the course of the trial the monkeys were required to fixate the target at the center of the display.

Speed Discrimination Task

During this task (Figure 1B), which was cued by a small fixation target in the form of a small triangle, the monkeys compared speeds of sample and test, and the speed differences between them bracketed each animal's threshold. The base speed in the speed task matched the speed used during the direction discrimination task to allow the direct comparison of stimulus responses during the two tasks. On each trial, the two stimuli moved either in the preferred or the antipreferred direction for a given neuron determined during the direction task, and on each trial one or both stimuli moved at a base speed (usually 2°/s or 4°/s) or at a comparison speed. The comparison stimuli used during each session were selected to bracket the threshold, defined as the stimulus value at 75% correct performance. Example psychometric functions measured for both monkeys, shown in Figure 1E, illustrate the similarity in the performance of the two animals.

Passive Fixation Task

During this task (Figure 1C), cued by a fixation target in the form of a small cross, stimulus conditions were identical to those used during the direction discrimination task, i.e., each trial consisted of two sequential stimuli (sample and test) separated by a 1500 ms delay. However, the monkeys were not required to report their perceptual decision by pressing buttons and were rewarded at the end of each trial as long as they maintained fixation.

Physiological Recordings

The recording sites in the PFC were selected from structural MRI scans. Recording procedures were similar to those used previously (Zaksas and Pasternak, 2006). During each session, a single tungsten microelectrode (0.8–3 MΩ; Alpha Omega Engineering, Alpharetta, GA) was lowered into cortex through a steel guide tube positioned in a cilux grid (Crist et al., 1988). The guide tube touched the dura but did not penetrate it. Waveforms from single neurons were isolated and recorded using a Multichannel Acquisition Processor system (Plexon, Dallas, TX). The raw field potential was filtered from 150 hz to 9 kHz. Waveforms were sampled and recorded at 40 kHz and the duration of each recording was set to match individual waveforms starting 100–200 μs before crossing of the negative threshold and continuing for 600–800 μs after, dependent upon the duration of the isolated unit. All recorded single units were separated online during the performance of the search task and further analyzed offline for goodness of separation from noise.

Waveform Analysis

During all recordings thresholds were manually set at the tail of the noise distributions. The average waveform for each recording was interpolated with a spline fit to a precision of 2.5 μs (www.snl.salk.edu/~jude/waveform_public/). Based on the differences in waveform durations between inhibitory interneurons and pyramidal neurons, revealed by previous intracellular recordings (Contreras and Palmer, 2003; McCormick et al., 1985), we classified our neurons by measuring the time between the trough and the peak of the spline fit to the mean waveform for each recording. Using these durations we divided neurons into two classes: NS putative inhibitory interneurons with spike durations of <200 μs, and excitatory BS putative pyramidal cells with spike durations >200 μs, an approach previously used by Mitchell et al. (2007). For further assurance that this metric provided us with two distinct groups of waveform durations, we performed Hartigan's dip test (Hartigan and Hartigan, 1985) on the distribution of spike durations. The test revealed significant bimodal distribution of the spike durations ($p = 0.02$) indicative of two distinct neuronal populations. In addition to waveform duration, we also took into account temporal patterns of spiking activity in our criteria and identified the chattering neurons, excitatory pyramidal cells characterized by short-duration action potentials and high-frequency bursts of activity (for details see Results).

Cell Selection

We searched for neurons with task-related activity while the monkeys performed a coarse direction discrimination task in which the directions of sample and test were either the same or differed by 90°. During this phase, neurons were selected for further study if they showed task-related activity in any period of the trial (sample, delay, or test). Task-related activity was defined as a significant deviation in firing rates from baseline activity recorded during the last 200 ms before sample onset. The significant activity was determined by sliding a 200 ms window in 100 ms steps throughout the response ($p < 0.01$; Mann-Whitney U test). In the current study, only neurons with significant task-related activity within 500 ms of sample or test onset were used for analysis.

Data Analysis

Analyses of spike data and statistical tests were performed using MATLAB (Mathworks, Natick, MA) and Excel (Microsoft, Redmond, WA). For the purposes of visual inspection, as seen in the example plots in Figure 2, the activity of each neuron during each behavioral session was plotted as a spike density function, generated by convolving the spike train with a Gaussian probability function (1 ms steps, $\sigma = 20$ ms). The firing rate at different stages of the task was analyzed by computing the mean number of action potentials over a given epoch in repeated presentations.

Direction Selectivity

Preferred direction was first identified during a separate direction discrimination task (search task) consisting of 40–60 trials in which eight directions of motion were presented as a sample or the test. The preferred direction was determined by computing a vector average of the mean firing rates in response to each stimulus direction. The opposite direction was termed antipreferred. Once identified in the search task, these directions were used in all subsequent tasks, the direction and speed accuracy tasks, and the passive fixation task. Baseline activity was measured during the last 200 ms of a 1000 ms fixation period immediately preceding the sample. Activity was analyzed by sliding a 100 ms window across the spike train in 10 ms steps. This window was used to identify task-related activity and selectivity.

ROC analysis was used to quantify DS by computing the AROC generated for each data set. The values were calculated for a 100 ms window slid in 50 ms increments along the spike train. The significance of each ROC value was established by a permutation test randomly redistributing firing rates for all the trials into preferred and antipreferred groups, regardless of the actual sample or test direction associated with each trial. An ROC value was then calculated from the redistributed groups, and the process was repeated 2000 times, creating a distribution of ROC values. The actual ROC value was deemed significant if it fell in the top or bottom 2.5% of the distribution ($p < 0.05$, two-tailed t test). An ROC value significantly greater than or less than 0.5 indicated that the firing rates were reliably higher in response to the preferred or the antipreferred direction, respectively. The time of emergence of DS was determined by sliding a 100 ms window in 10 ms increments across each response and testing for a significant difference between the rates elicited by the preferred and the antipreferred directions. Onset of DS was taken as the center of the first bin of at least six consecutive significant bins of activity. The offset of DS was the center of the first of at least eight consecutive bins of activity that did not reach statistical significance. The duration of DS was taken as the difference between the onset and the offset of DS.

Task Effects on Direction Selectivity

The change in DS across tasks was quantified by computing for each neuron a task index as the difference between the two AROC curves ($AROC_{speed/passive} - AROC_{direction\ task}$). To access the significance of task effect on DS for individual neurons, we performed a two-way ANOVA with direction (preferred or antipreferred) and task as the main factors. Neurons with significant task effects were those that showed a significant interaction effect between direction and task at $p < 0.05$. Within each cell type, differences in DS across tasks were evaluated by a Wilcoxon signed-rank test ($p < 0.05$). Differences in task effects between the two cell types were assessed by a Mann-Whitney U test ($p < 0.05$) for a difference in median task effect between cell types.

Latency of Task Effect

The timing of task effects was determined by measuring the latency of the average effect for the population of NS and BS neurons. We used two approaches to define the latency of the effect. In one approach, the task effect was calculated by stepping a 100 ms window at 1 ms intervals through the response and calculating significance values to evaluate whether the mean task effect for NS and BS neurons significantly deviated from 0 (Mann-Whitney U test, $p < 0.05$). The latency for each cell class was taken as the center of the first of at least 25 consecutive significant bins. One of the drawbacks of this approach is that this measure is likely to be affected by the difference in the amplitude of the effects being compared, as was the case with task effects during the speed task. The second approach avoids this problem by using a half-height method. With this approach the latency was taken as the center of the first of at least 20 consecutive bins where the mean task effect exceeded half the value of its maximum. The significance of the difference in latencies between cell classes determined with this method was evaluated using a two-sample bootstrap hypothesis test (Efron and Tibshirani, 1993). This was done by pooling the data sets for all neurons and randomly sampling, without replacement, the two data sets equal in size to the NS and BS samples. A difference in latency from this random sample was calculated. This process was repeated 2000 times and the difference in latency was considered significant if the observed value fell within the top or bottom 2.5% of the bootstrapped distribution.

Task Effects on Responses to Each Direction

We evaluated how responses to the preferred and antipreferred direction changed across tasks (shown in Figures 6, 7, and S4) by sliding a 200 ms bin in 25 ms increments along the spike train of individual neurons. In each task, the mean activity during the 200 ms preceding the sample or test was subtracted from the response. The difference in these baseline-subtracted rates was then divided by the sum of the average response 100–500 ms after stimulus onset in both tasks. The significance of average task effects for preferred or antipreferred responses recorded during 100–500 ms was evaluated on a cell-by-cell basis by Mann-Whitney U test ($p < 0.05$).

SUPPLEMENTAL DATA

Supplemental data for this article include five figures and can be found at http://www.cell.com/neuron/supplemental/S0896-6273(09)00932-5.

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